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AN OBSERVATIONAL STUDY ON- MANAGEMENT OF ANEMIA IN CKD USING ERYTHROPOIETIN ALPHA

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ABSTRACT

AIMS: To assess the efficacy of erythropoietin alpha in management of anemia of CKD.

OBJECTIVES

- ***To treat anemia of CKD using erythropoietin alfa.***
- ***To assess treatment intensification.***
- ***To assess adherence to medications.***
- ***To monitor GFR rate.***
- ***To study the effect of treatment on stages of CKD.***

Methodology: A Suitably designed data collection form was prepared for the patients which includes demographic details of the patients such as age, gender, weight, laboratory data of blood, biochemistry, USG of abdomen, treatment pattern, follow up and Questionnaires on lifestyle changes occupation and side effects. Statistical analysis was performed by using mean, standard deviation two tailed paired T-test, class intervals and percentage in excel. The comparison between the study groups were performed with the use of two tailed t-test.

Results: A total of 250 patients were enrolled in study from single centre. According to gender wise 250 patients were enrolled, 158(63%) males and 92(37%) females. According to Age wise category the highest prevalence of CKD was observed between61-70(24%) years. Based on family history 109(43.6%) do not have a family history, HTN with 70 (28%) and DM with40(16%). Based on the distribution of area 194(77.6%) are rural and 56(22,4%) are urban followed by 82% literate and 18% illiterate. According to symptoms, 89.6% were SOB, followed by 76.4%of pedal edema, 51.6% of loss of appetite. Out of 250 patients, the existing medical comorbities were highest prevalent in HTN with 42% followed by HTN+DM with 23.2%, the least were UTI and AKI with 2.8%. Among 250 patients 137(55%) undergo dialysis. Based on the class of drugs 177(70.8%) use calcium channel blockers and 175(70%) use diuretics. Among 250 patients 99% were anemic and 1% were non-anemic, followed by 156(63.1%) were male and 91(36.8%) were female. Based on stage of CKD, out of 250 patients 202(80.8%) belong to ESRD

Conclusion: This study concludes that erythropoietin alfa was effective in treating anemia in CKD patients. The drug effectively managed the Hb levels above 12g/dl in both dialysis and non dialysis patients. The drug promisingly improved the quality of life and also decreased the probability of comorbidities due to anemia in CKD patients like shortness of

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breath and cognition. In our study, the drug is comparatively more effective than packed cell transmission and shows long term improvement on Hb percentage in blood. The target Hb levels of 11-12 g/dl was achieved after 2 weeks of treatment using SC erythropoietin alfa thrice weekly. Erythropoietin alfa was well tolerated with mild to moderate side effects.

KEYWORDS: CKD (Chronic Kidney Disease), Anemia, Dialysis, Erythropoietin Alpha, Dialysis, Hb (Hemoglobin) & QOL (Quality Of Life)

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INTRODUCTION

Anemia is defined as a reduction in one or more of the major red blood cell measurements: hemoglobin concentration, hematocrit, or RBC count. The World Health Organization defines anemia as a hemoglobin level less than 13 g/dL in men and postmenopausal women, and less than 12 g/dL in premenopausal women. The NKF defines anemia as a hemoglobin of less than 13.5 g/dL in men and less than 12 g/dL in women.

CAUSES OF ANEMIA IN CKD

Decreased erythropoietin production.

Increased hepcidin leads to iron sequestration in macrophages, iron-restricted erythropoiesis, resistance to erythropoietin.

Iron deficiency due to blood loss and hepcidin mediated decrease in intestinal iron absorption.

Shortened RBC life span due to inflammation and uremia.

Suppression of erythropoiesis by inflammatory cytokines.

- Low B12 and folate.
- Poor lifestyle maintenance.

TREATMENT OF ANEMIA IN CKD

Benefits

- Increased exercise tolerance.
- Increased quality of life.
- Decreased morbidity and mortality.
- Reduced left ventricular hypertrophy.

Treatment Options

- Iron supplementation.
- Erythropoiesis stimulating agents.
- Blood transfusion.

- Folic acid and vit B12 supplementation.

Erythropoiesis Stimulating Agents

- 1st generation: Erythropoietin alfa and Erythropoietin beta.
- 2nd generation: Darbapoietin.
- 3rd generation: Continuous Erythropoietin Receptor Activator.

Erythropoietin Alfa

Erythropoietin alfa is a 165-amino acid erythropoiesis stimulating agent manufactured by recombinant DNA technology.

This drug stimulates erythropoiesis similarly as endogenous epoietin.

PHARMACOKINETICS

Absorption: Maximum peak plasma concentration seen in 20-25 hrs.

Bioavailability: 20-40%.

Vd: 40-63.80 ml/kg.

Metabolism: Lymphatic system or reticuloendothelial scavenging pathway.

Route of elimination: EPOR-R-expressing cells, lymphatic system and very small amount in urine.

Half life: 4-13 hrs.

AVERAGE RATE OF Hb RISE IN 2 WEEKS

Table 1

Starting dose (thrice Weekly IV / SC)	Hb increase in 2 Weeks
50 units/Kg	0.5 g/dL
100 unts/Kg	0.8 g/dL
150 units/Kg	1.2 g/dL

Contraindications

Uncontrolled HTN, Pure red cell aplasia, Allergic reaction to erythropoietin alfa, infants and lactating women

Side Effects

Joint and muscle pains, High blood sugar, Low potassium levels in blood, Soreness and itching in mouth, Respiratory infections, Weight loss

METHODOLOGY

The present study was conducted at **VISWAS SUPER SPECIALITY HOSPITAL,** Hanmakonda. This hospital is situated in the heart of the city with the objective of providing pharmacological treatment for kidney, diabetic and HTN related problems also comprises of a Dialysis unit. Our study is a hospital based observational study.

This study was carried out for 6 months (October-march) 2019-2020 with a sample size of 250 patients at this hospital. The study includes patients with CKD & ESRD with anemia patients receiving erythropoietin alpha, patients

receiving packed cell transfusion, patients not receiving any treatment for anemia of CKD patients not meeting the inclusion criteria will not be included in the study. Patient demographics (age, gender, diet, and occupation), medical history, social history and diagnostic data and follow-up will be conducted for next clinic visits. The Source of data is from patients, patient case reports, prescriptions and physicians, patient relatives and Lab data. The statistical analysis was performed by using mean, standard deviation two tailed paired T-test, class intervals and percentage in excel. The comparison between the study groups were performed with the use of two tailed t-test and class intervals was used for categorical measures.

RESULTS

- **Distribution based on Age and Gender:** Out of 250 study population, patients were divided into various groups according to their age and gender. Highest prevalence of CKD was observed in the age group between 61-70 years (24%) followed by 51-60 years (21.6%) and the least prevalence was observed between 10-20 years (0%) followed by 21-30 years (8%).
- **Distribution based on Gender:** Out of 250 patients, 63% were male and 37% were female. Highest prevalence was observed in males
- **Distribution of data based on family history of Kidney Diseases:** Out of 250 patients, the majority of patients 43.6% do not have a family history of kidney diseases, 12.4% of patients presented a family history of Kidney diseases, 28% of patients presented with a family history of HTN, 16% patients presented with a family history of DM
- **Area wise distribution of data:** Out of 250 patients, 77.6% of patients belong to rural areas and 22.4% of patients belong to urban areas. The highest prevalence was observed among the rural population compared to the urban population.

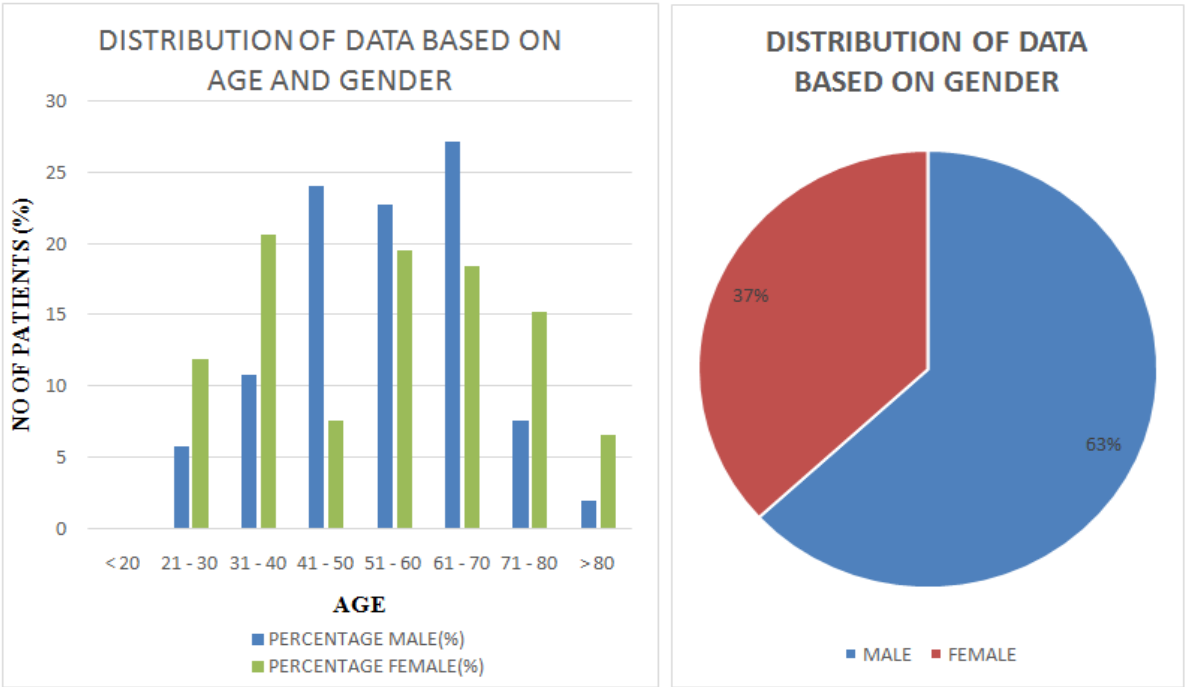

Figure 1

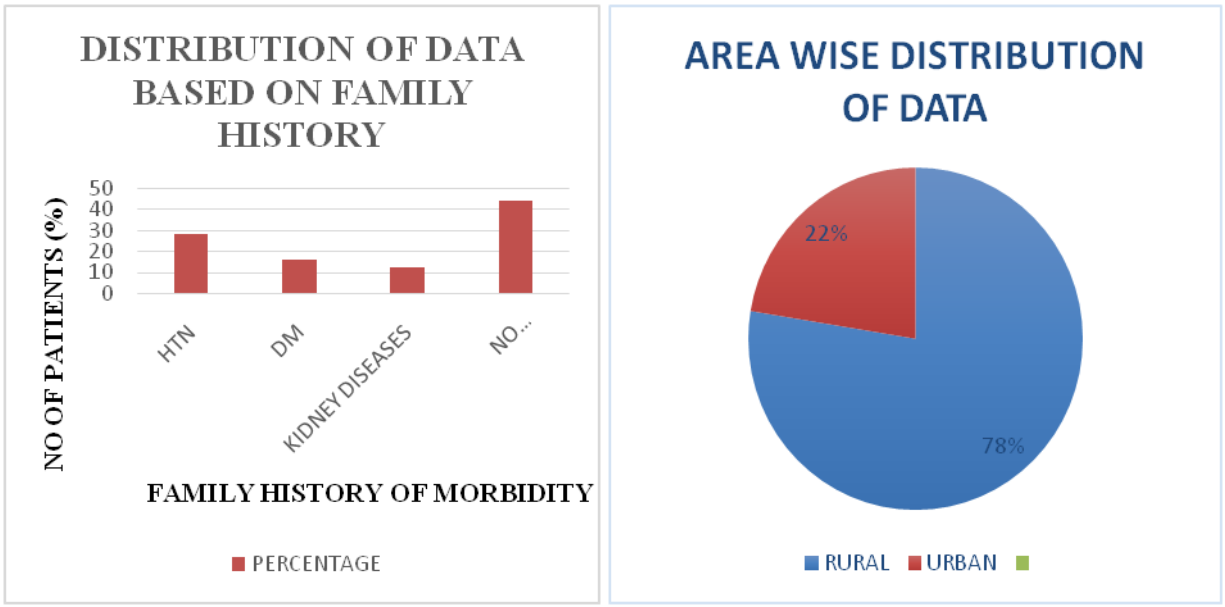

Figure 2

- **Distribution of data based on literacy rate:** Out of 250 patients 82% patients were literate and 18% patients were illiterate.
- **Presenting symptoms of patients with Chronic Kidney Disease:** Out of 250 CKD patients, SOB is the most common presenting symptoms (89.6%), followed by pedal edema (76.4%), loss of appetite (51.6%) and fever (14%), burning micturition & anuria (10.4%) respectively.
- **Existing medical comorbidities in patients with Chronic Kidney Disease:** Out of 250 patients, highest prevalent comorbidity observed was Hypertension (42%), followed by Hypertension + DM (23.2%) and least co-morbid condition was UTI (2.8%) and AKI (2.8%).

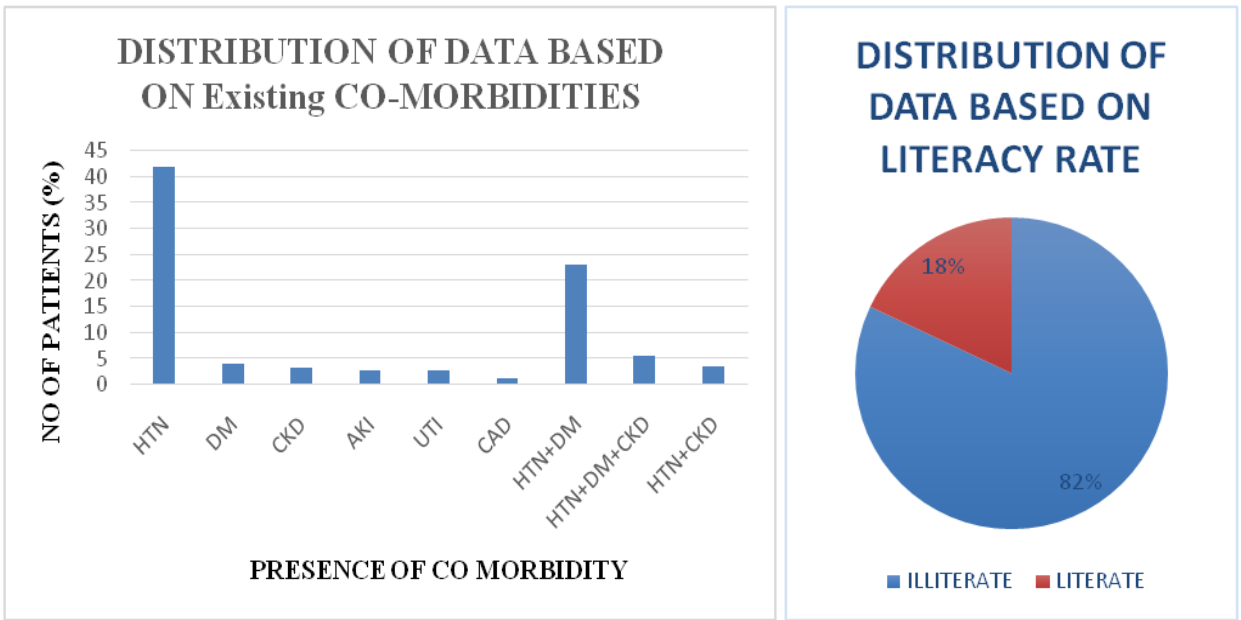

Figure 3

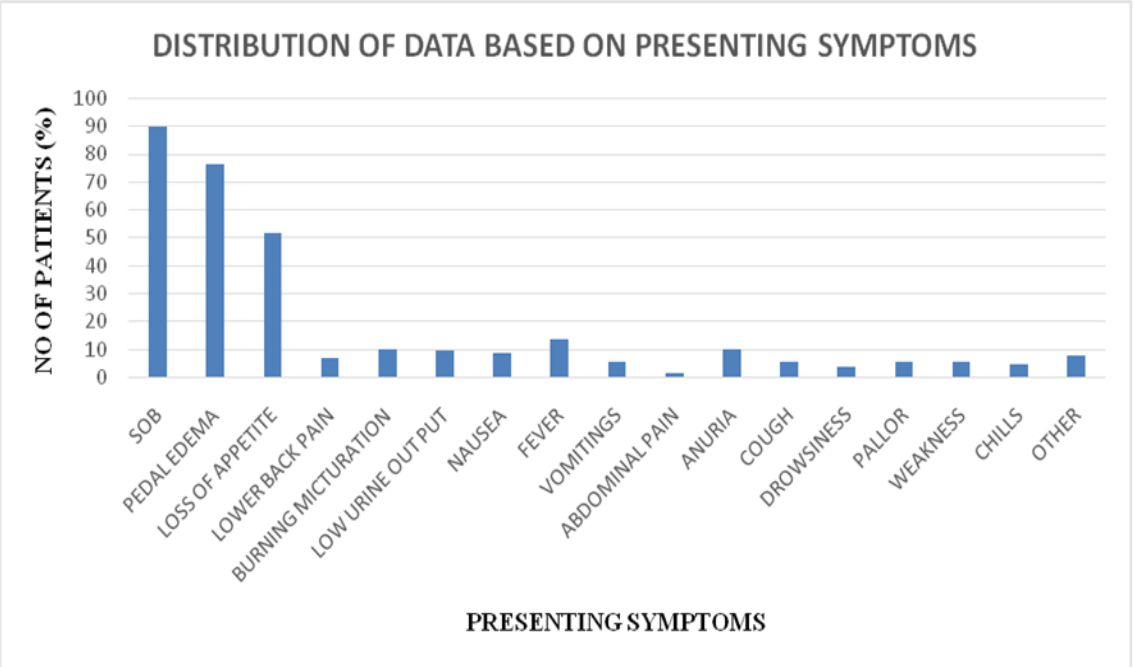

Figure 4

- **Patients Undergoing Dialysis:** Out of 250 CKD patients percentage of patients undergoing dialysis where higher (55%), and patients not undergoing dialysis were lower (45%).
- **Distribution of data based on the class of drugs administered:** Out of 250 patients, 70.8% of patients were administered calcium channel blockers, 70% of the patients were administered diuretics, 58.8% of the patients administered H2 blockers, 55.2% of the patients administered PPI's.
- **Severity of anaemia in CKD:** Out of 250 patients 247 patients were anaemic, among them 91 (36.8%)were female, 156(63.1%) were male.

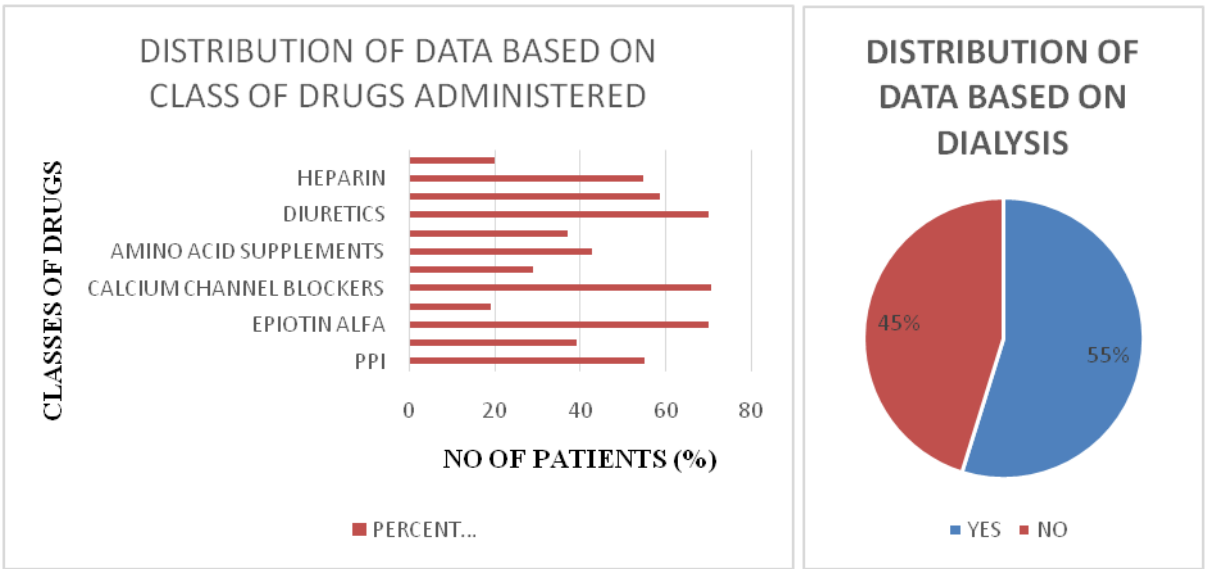

Figure 5

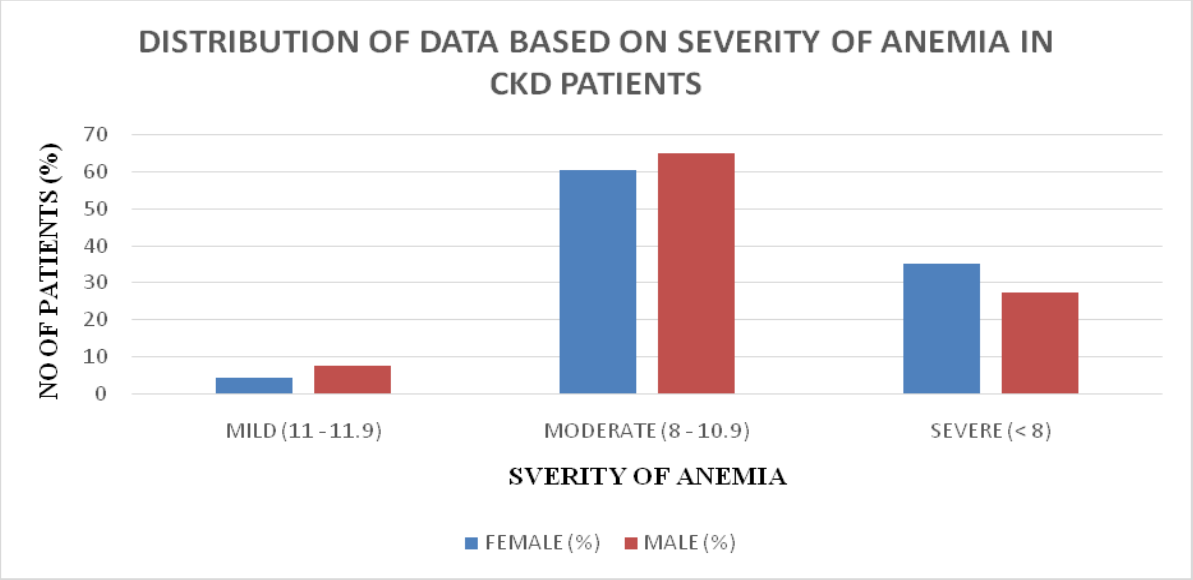

Figure 6

Distribution Of data based on stage of CKD: Out of 250 patients 2 (0.8%) have normal GFR, 3 (1.2%) have slightly decreased GFR, 4 (1.6%) have mild CKD, 11 (4.4%) have moderate CKD, 28 (11.2%) have severe CKD, 202 (80.8%) have ESRD.

Table 2

Stage of CKD	Male (%)	Female (%)	Total (%)
Normal (90)	2 (0.8)	0	2 (0.8)
Slight (60-89)	3 (1.2)	0	3 (1.2)
Mild (45-59)	2 (0.8)	2 (0.8)	4 (1.6)
Moderate (30-44)	8 (3.2)	3 (1.2)	11 (4.4)
Severe (15-29)	18 (7.2)	10 (4)	28 (11.2)
Esrd/on dialysis (<15)	78 (31.2)	124 (49.6)	202 (80.8)
Total	**44.4**	**55.6**	**250 (100)**

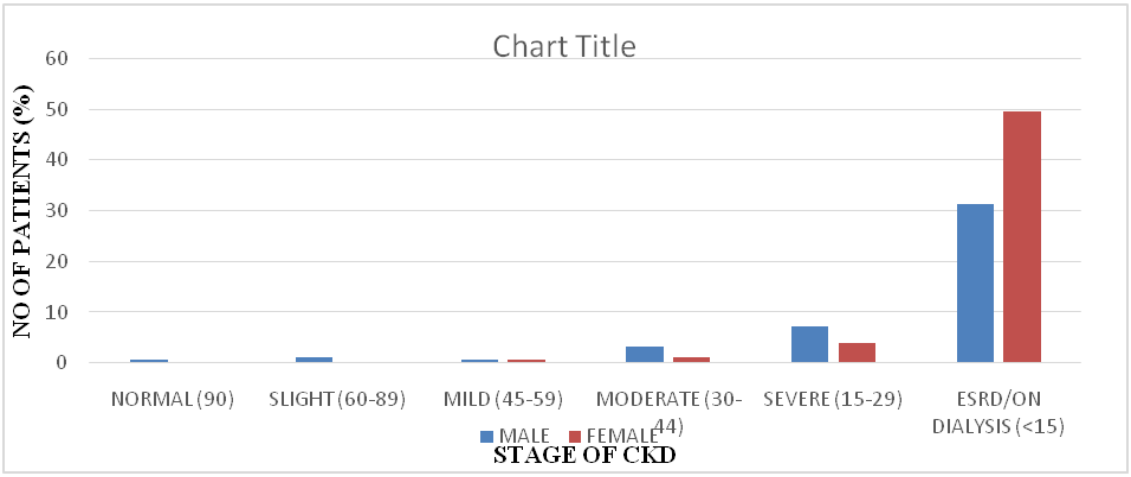

Figure 7

DISCUSSIONS

Anemia in CKD is typically normocytic, normochromic and hypo-proliferative. Anemia in patients with CKD is multifactorial in origin. Primarily associated with relative erythropoietin deficiency as GFR rate falls down. As kidney diseases progress, anemia increases in prevalence, affecting nearly all patients with stage 5 CKD. Anemia in CKD is associated with reduced quality of life and increased hospitalization, cognitive impairment and mortality. Treatment with epoietin alfa has been shown to enhance the quality of life by decreasing the need for hospitalization, cognitive impairment and mortality.

The present study was designed to study the efficacy of erythropoietin alfa in the management of anemia in CKD. The drug was given to the patient SC/IV, three/two times in a week at a dose of 2000 IU. Hb levels of patients were observed throughout the treatment period to check the improvement in the management of anemia. Patients on dialysis were given SC dosing after the session thrice/twice weekly. The dosing and frequency was decided in non dialysis patients based on the severity of anemia.

In a study conducted by Melissa E.Staffer et al 2014, stated that anemia was present in 15.4% people with any stage of CKD. In a study conducted byr Bruce Robinson et al 2007, they found that 60% of patients had anemia. In a study conducted by Muhammad Salman et al 2016, stated that anemia was present in 75.8% of study population of which 47.7% were mild, 32.2% were moderate and 20% were severe. In our study, we observed that 98% of the study population is anemic and 7.5%, 65%, 27.5% were observed to be mild, moderate and severe respectively. A possible explanation would be, we have greater proportion of ESRD patients in our study population who require regular dialysis. It is also proven that the prevalence of anemia increases with the progression of disease.

In studies conducted by (Robert Benz et al, Amir Hayat et al, Eschbach JW et al) they concluded that recombinant erythropoietin alfa was effective and safe (when base line Hb is maintained 11-12 g/dl) in treating anemia of CKD and showed improvement in quality of life, decreased hospitalization in comparison with packed cell transfusion cases. Similarly, in our study, we observed that erythropoietin alfa is effective in managing anemia of CKD and also shows better quality of life.

In our study number of male CKD patients were more than female patients, as was found in other studies (Smithasontakke et al 2015, CS. Manju et al). Male being more susceptible to CKD might have something to do with a greater prevalence of smoking and drinking in men, as compared to women.

Other studies conducted in our country (Phisittvejakamma et al 2017, CS Manju et al 2016 and Saurav Ghimire et al 2017) showed that CKD is more common in the age group of 50-85 years. In the present study, most of the patients were in the age group of 61-70 years. A possible explanation is decreased functioning of organs and high risk of complications with advancing age.

Previous studies (Dena. K Rifkin et al 2010, CS Manju et al 2016 and Phisittvejkamma et al 2017) indicated bank HTN and DM are the major risk factors of CKD similarly in this study out of 250 study population we identified 42% HTN, 23.2% HTN and DM, 4% DM patients. Other comorbidities observed are AKI, UTI and Renal calculi.

Mitheshsingh et al 2017, stated that 87% of CKD patients were urban and 13% from rural areas. Similarly, we

observed that 77.6% of CKD patients were from rural areas and 22.4% from urban. Majority of cases were observed from rural areas due to a lack of awareness regarding the disease.In our study out of 250 study population 82% were illiterate and 18% of the population was literate.

CONCLUSIONS

This study concludes that erythropoietin alfa was effective in treating anemia in CKD patients. The drug effectively managed the Hb levels above 12g/dl in both dialysis and non dialysis patients. The drug promisingly improved the quality of life and also decreased the probability of comorbidities due to anemia in CKD patients like shortness of breath and cognition. In our study, the drug is comparatively more effective than packed cell transmission and shows long term improvement on Hb percentage in blood. The target Hb levels of 11-12 g/dl was achieved after 2 weeks of treatment using SC erythropoietin alfa thrice weekly. Erythropoietin alfa was well tolerated with mild to moderate SE's.

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